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The opinion in support of the decision being entered today was *not* written for publication and is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte AUDREY GODDARD, PAUL J. GODOWSKI,
AUSTIN L. GURNEY, VICTORIA SMITH, and WILLIAM I. WOOD

Appeal 2006-1469
Application 10/123,212
Technology Center 1600

Decided: April 30, 2007

Before TONI R. SCHEINER, ERIC GRIMES, and LORA M. GREEN,
Administrative Patent Judges.

GREEN, *Administrative Patent Judge.*

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 72-79 and 82-84. We have jurisdiction under 35 U.S.C. § 6(b). Claims 72 and 77 are representative of the claims on appeal, and read as follows:

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72. An isolated polypeptide having at least 80% amino acid sequence identity to:
(a) the amino acid sequence of the polypeptide of SEQ ID NO:14;
(b) the amino acid sequence of the polypeptide of SEQ ID NO:14, lacking its associated signal peptide; or
(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203577,
wherein the nucleic acid encoding said polypeptide is overexpressed in colon, lung or prostate tumor cells.

77. An isolated polypeptide comprising:
(a) the amino acid sequence of the polypeptide of SEQ ID NO:14;
(b) the amino acid sequence of the polypeptide of SEQ ID NO:14, lacking its associated signal peptide; or
(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203577.

Claims 72-79 and 82-84 stand rejected under 35 U.S.C. § 101 as not being supported by either a specific and substantial utility or a well-established utility. Claims 72-76, 83, and 84 stand rejected under 35 U.S.C. § 112, first paragraph, as not being enabled by the specification, and claims 72-76, 83, and 84 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description. Finally, 72-74, 83, and 84 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Young,¹ and claims 72-75, 83, and 84 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Stanton.²

We Affirm-In-Part.

¹ Young, US Patent No. 6,525,174 B1, issued February 25, 2003.

² Stanton, US Pub. No. 2002/0110804 A1, published August 15, 2002.

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UTILITY

ISSUE

The Examiner contends that the Specification fails to establish a specific and substantial utility or a well-established utility of the polypeptide of SEQ ID NO:14.

Appellants contend that Example 30 presents microarray data demonstrating that the polypeptide of SEQ ID NO:14 is a diagnostic marker for colon, lung, and prostate tumors.

The issue is thus whether the microarray data presented in Example 30 of the Specification is sufficient to establish a specific and substantial utility or a well-established utility for the polypeptide of SEQ ID NO:14?

FACTS

The Examiner rejected claims 72-79 and 82-84 under 35 U.S.C. § 101 as not being supported by either a specific and substantial asserted utility or a well-established utility (Answer 4).

The Examiner notes that the Specification discloses the polypeptide of SEQ ID NO:14 (PRO1866), the nucleic acid sequence encoding it (SEQ ID NO:13), as well as antibodies against the polypeptide. (*Id.*)

As to a well-established utility, the Examiner asserts that the prior art does not demonstrate that the polypeptide of SEQ ID NO:14, the nucleic acid encoding the polypeptide or an antibody that binds to the polypeptide, has "any well-established biological functions or any physiological significance." (*Id.* at 4-5.)

Next, as to a specific and substantial utility, the Examiner references Table 8 of the Specification, which states that the polypeptide is

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significantly overexpressed in colon, lung, or prostate tumors compared to a non-cancerous human tissue control. (*Id.* at 5.) The Examiner also notes that the statement is based on a microarray analysis, which measures mRNA levels, and not overexpression of the polypeptide of SEQ ID NO:14 itself. (*Id.*) According to the Examiner:

There is no sufficient information or experimental data presented on whether the polypeptide or the nucleic acid of the present invention can serve as a reliable diagnostic marker for colon, lung or prostate tumors; there is no statistical analysis of the expression data. Moreover, the assay does not establish a causative link between the polypeptide (or nucleic acid) of the present invention and colon, lung or prostate tumors. Without such critical information, one skilled in the art would not be able to use the molecule of the present invention as a diagnostic marker or as a therapeutic target for treatment of colon, lung or prostate tumors without undue experimentation. Accordingly, the results in Table 8 obtained based upon the assay described in Example 30 only serve as the beginning point for further research on the biological functions or physiological significance of the polypeptide of SEQ ID NO:14 or the nucleic acid encoding the polypeptide, and does not provide a specific and substantial utility for the present invention.

(*Id.* at 5-6.)

Appellants argue that patentable utility is demonstrated by Example 30 of the Specification (Br. 4). According to Appellants, Example 30 demonstrates that the gene encoding the polypeptide of PRO1866 (SEQ ID NO:14) "showed significant overexpression in colon, lung, and prostate tumors as compared to a universal normal control," demonstrating "that the PRO polypeptides of the present invention are useful . . . as diagnostic markers for the presence of one or more cancerous tumors" (*Id.*)

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Appellants argue further that it is legally incorrect for the Examiner to require specific data, statistical analysis, and further details before accepting the utility set forth in the Specification, as the law is clear that the Examiner must accept Appellants' assertion of utility if that assertion would be credible to one of ordinary skill. (*Id.* at 4-5.)

Appellants assert that the Examiner has used an improper standard in asserting that mRNA levels do not necessarily correlate with the protein level and that protein levels cannot be accurately predicted from mRNA levels. (*Id.* at 6.) The evidentiary standard to be used during examination is preponderance of the evidence under the totality of the circumstances, and thus, Appellants argue, the Examiner "must establish that it is *more likely than not* that one of ordinary skill in the art would doubt the truth of the statement of utility," which "is a much lower standard than a 'necessary' correlation or 'accurate' prediction, and is clearly met for the invention claim." (*Id.* (emphasis in original)).

Moreover, Appellants rely on the Declaration of Dr. Paul Polakis, which states that "*in general, there is a correlation between mRNA levels and polypeptide levels.*" (Br. 6 (emphasis in original)). Appellants also rely on the Declaration of Dr. Victoria Smith, which states that "*microarray analyses actually performed in my laboratory have shown that when molecules are identified as being overexpressed in a human tumor sample of epithelial origin relative to the 'universal normal control'*³ *sample, in a majority of cases, that molecule is also confirmed as being overexpressed in*

³ The "universal" epithelial control sample is prepared by pooling non-cancerous human tissues of epithelial origin, including liver, kidney, and lung (Br. 12).

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the human tumor tissue sample relative to its human tissue counterpart" (Br. 6 (emphasis in original)). Appellants aver that the two declarations support the assertion of utility in the Specification, *i.e.*, that the PRO1866 polypeptide (SEQ ID NO:14) "is reasonably expected to be overexpressed in colon, lung and prostate tumors and can be used as a cancer diagnostic marker." (*Id.* at 6-7.)

The Specification is drawn to the identification and isolation of novel DNA and to the recombinant production of polypeptides (Specification 1).

Example 30 on page 134 of the Specification is drawn to microarray analysis to detect PRO polypeptides in cancerous tumors.

According to the Specification:

In the present example, cancerous tumors derived from various human tissues were studied for PRO polypeptide-encoding gene expression relative to non-cancerous human tissue in an attempt to identify those PRO polypeptides which are overexpressed in cancerous tumors. Two sets of experimental data were generated. In one set, cancerous human colon tumor tissue and matched non-cancerous human colon tumor tissue from the same patient ("matched-colon control") were obtained and analyzed for PRO polypeptide expression using . . . microarray technology. In the second set of data, cancerous human tumor tissue from any of a variety of different human tumors was obtained and compared to a "universal" epithelial control sample which was prepared by pooling non-cancerous human tissues of epithelial origin, including liver, kidney, and lung. mRNA isolated from the pooled tissues represents a mixture of expressed gene products from these different tissues. Microarray hybridization experiments using the pooled control samples generated a linear plot in a 2-color analysis. The slope of the line generated in a 2-color analysis was then used to normalize the ratios of (test:control detection) within each experiment. The normalized ratios from various experiments were then compared and used to identify clustering

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of gene expression. Thus, the pooled "universal control" sample not only allowed effective relative gene expression determinations in a simple 2-sample comparison, it also allowed multi-sample comparisons across several experiments.

In the present experiments, nucleic acid probes derived from the herein described PRO polypeptide-encoding nucleic acid sequences were used in the creation of the microarray and RNA from the tumor tissues listed above were used for the hybridization thereto. A value based upon the normalized ratio:experimental ratio was designated as a "cutoff ratio". Only values that were above this cutoff ratio were determined to be significant. Table 8 below shows the results of these experiments, demonstrating that various PRO polypeptides of the present invention are significantly overexpressed in various human tumor tissues as compared to a non-cancerous human tissue control. As described above, these data demonstrate that the PRO polypeptides of the present invention are useful not only as diagnostic markers for the presence of one or more cancerous tumors, but also serve as therapeutic targets for the treatment of those tumors.

(*Id.* at 134-35.)

As to PRO1866, the Specification presents Table 8, which states that PRO1866 is overexpressed in colon tumor, prostate tumor, and lung tumor, as compared to universal normal control. (*Id.* at 135.)

The Declaration of Dr. Paul Polakis, dated September 9, 2005, states in paragraphs 4 and 5 that, based on experience with other gene transcripts that are present in human tumor cells at significantly higher levels than in corresponding normal human cells, it has been observed "that there is a strong correlation between changes in the level of mRNA present in any particular cell type and the level of protein expressed from that mRNA in that cell type. In approximately 80% of our observations we have found that increases in the level of a particular mRNA correlates with changes in the

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level of protein expressed from that mRNA when human tumor cells are compared with their corresponding normal cells."

The Declaration of Dr. Victoria Smith at paragraph 5, dated September 9, 2005, states that the comparison of mRNA expression levels in human tumor tissues to mRNA expression levels in a sample prepared by pooling non-cancerous human tissues of epithelial origin "is extremely informative and provides a strong basis for the diagnostic determination of cancer in humans."

PRINCIPLES OF LAW

The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. See *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995). ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.").

The Court of Appeals for the Federal Circuit addressed the utility requirement in *In re Fisher*, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005). The *Fisher* court interpreted *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966), as rejecting a "de minimis view of utility." 421 F.3d at 1370, 76 USPQ2d at 1229. The *Fisher* court held that § 101 requires a utility that is both substantial and specific. *Id.* at 1371, 76 USPQ2d at 1229. The court held that disclosing a substantial utility means "show[ing] that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to

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satisfy the 'substantial' utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public." *Id.*, 76 USPQ2d at 1230.

The court held that a specific utility is "a use which is not so vague as to be meaningless." *Id.* In other words, "in addition to providing a 'substantial' utility, an asserted use must show that that the claimed invention can be used to provide a well-defined and particular benefit to the public." *Id.*

ANALYSIS

We find that the microarray data presented in Example 30 of the Specification is sufficient to establish a specific and substantial utility for the polypeptide of SEQ ID NO:14, and the rejection is reversed.

The microarray data demonstrates that mRNA for the PRO1866 polypeptide (SEQ ID NO:14) is overexpressed in colon tumor, prostate tumor, and lung tumor, as compared to universal normal control. Thus, the polypeptide of SEQ ID NO:14 has a significant and presently available benefit to the public as a tumor marker.

We have considered the Examiner's assertions that microarray analysis measures mRNA levels, and not overexpression of the polypeptide of SEQ ID NO:14 itself. As demonstrated by the Polakis and Smith Declarations, however, there is a strong correlation between mRNA levels and protein expression, and the Examiner has not presented any evidence specific to the PRO1866 polypeptide to refute that.

Finally, the use of the PRO1866 polypeptide as a cancer marker is sufficient to demonstrate utility, and there is no requirement that a causative

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link between the polypeptide (or nucleic acid) of the present invention and colon, lung or prostate tumors be demonstrated.

ENABLEMENT

ISSUE

The Examiner contends that the disclosure does not enable one skilled in the art to practice the full genus of peptides encompassed by Appellants' claims.

Appellants contend that one skilled in the art could practice the full scope of the claimed invention, as the skilled artisan has a sufficiently high level of technical competence to identify sequences with at least 80% identity to SEQ ID NO:14, and the specification provides ample guidance such that one of skill in the art could readily test the nucleic acid encoding a variant polypeptide to determine whether it is overexpressed in colon, lung or prostate tumors by the methods set forth in Example 30.

Thus, the issue is does the Specification enable one skilled in the art to use the full scope of the PRO1866 (SEQ ID NO:14) variants of claim 72 without an undue amount of experimentation?